POINT-OF-CARE TESTING: CAN IT BE ADAPTED FOR THE FIELD ENVIRONMENT?

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SUMMARY

Technologic advances have made laboratory testing feasible at the bedside. Point-of-care testing (POCT) allows medical providers to assess a wide range of clinical conditions in a rapid fashion at the site of patient interaction. While POCT has begun to impact on the delivery of care in the hospital setting, its potential for use in remote, field environments or during aeromedical evacuation is just being realized. In the civilian setting, discussion of POCT focuses on regulatory guidance, cost effectiveness, and reimbursement. Little attention has been paid in the literature to expanding the use of these capabilities beyond the traditional hospital boundaries. In this paper, we will briefly review the development of POCT and the associated technology. In addition, we will discuss the potential role of POCT in the field using current technology. Finally, we will review the available literature on use of POCT in the field.

INTRODUCTION

When providing direct patient care in nontraditional settings, there occasionally arises the need to ascertain physiologic measurements which are difficult to obtain outside of the hospital environment. Rapid analysis of laboratory tests can be essential in the management of our patients, particularly the critically ill and injured. The availability of selected analytes such as glucose, electrolytes, hematocrit, blood gases, and pH can significantly affect the direction of treatment, prognosis, and triage decisions. The lack of this information can lead to the assumption of a "worst case" which will then drive triage and treatment decisions that may adversely impact the delivery of care to other patients and the need for evacuation.

The development of devices incorporating microchemistry, miniaturization, and microcomputerization has led us to a point where many of these desired tests can be performed real-time at the point of patient interaction. This capability is referred to as point-of-care testing (POCT). It would seem a simple answer to a complex clinical problem, but even in the traditional clinical setting, POCT is surrounded by controversy. Issues of regulation, quality management, and cost effectiveness often interfere with the establishment of a POCT system. In the field setting, there are even more questions regarding durability, reliability, and ease of use.

In this paper, we will review the development of POCT along with its associated technology. Using this information we will examine some of the currently available systems and their applicability for use in the field or during aeromedical evacuation. Finally, we will review the limited literature on POCT in the field to assess the overall utility of this technology for application in the, more often than not, hostile field environment.

POCT DEVELOPMENT

There has always been a desire on the part of clinicians to have immediate access to all of the variables which impact on our patient's diagnosis, treatment, and prognosis. Technologic advances continue to provide us with greater opportunities to have that information at our fingertips. Point-of-care testing has been available for many years. The monitoring of blood glucose concentrations through the use of reagent strips and subsequent techniques has been available since the 1970's (Ref 1). The Vietnam conflict with the resulting movement of large numbers of casualties led to early attempts to provide portable, miniaturized electrolyte analyzers (Fig 2). Concerns about the need to provide rapid evaluation of hematocrit and electrolytes in burn patients being moved through the aeromedical system was the prime motivating factor in these development efforts (Ref 2).

The real drive to bring POCT into a useful role was tied to the requirements of liver transplantation (Ref 3). In these cases, rapid changes in ionized calcium demanded an almost immediate knowledge of its level to direct appropriate therapy. This need exceeded even the capabilities of most "stat" laboratories and led to the introduction of whole blood biosensors directly into the operating room. The addition of bedside potassium and hemostasis testing following almost immediately.

This shift away from the traditional laboratory paradigm was quick to take hold in other areas. No longer did discrete specimens have to be collected, transported, centrifuged, analyzed, recorded, and transmitted back to the originator. The use of whole blood samples in portable, often hand held, instruments simplified the process to the point that relatively little training was required to produce consistent accurate results. The development of critical test clusters now provides valuable indicators of vital functions right at the bedside. As of 1995, approximately 83% of U.S. hospitals had hand-held POCT programs (Ref 4) and that number is probably 100% today. The addition of in vivo and ex vivo instruments to POCT has even further expanded our already plentiful capabilities.

**POCT TECHNOLOGY**

Conventional methods of diagnostic testing present several problems when dealing with critically ill or injured patients. Unnecessary process steps, prolonged turnaround times, and delayed results which are no longer relevant to the current patient condition contribute to delays in therapy. The improvements made in sensor technology over the last two decades now allow us to implement a patient-focused testing system. A chemical sensor consists of three basic elements: a sensing unit where recognition of the analyte occurs, a relay section that transmits the signal produced to the sensing unit, and a measurement instrument that interprets the signal and calculates its value (Ref 5). These new chemical biosensors can be broken down into two major categories: electrochemical or optical.

**Electrochemical Sensors**

Electrochemical sensors are able to measure blood gases, pH, electrolytes, and metabolites. These sensors produce a potential or current in response to their reaction with the analyte of interest. Ion-selective electrodes measure the free ion of interest in whole blood. They do so by use of ion-selective membrane coverings which extract or bind the ion creating a charge separation or electrical potential in proportion to the concentration. Electrodes of this type can be used to measure bicarbonate, sodium, potassium, ionized calcium, chloride, magnesium, pH, and the partial pressure of carbon dioxide (pCO₂).

Amperometric sensors produce current through oxidation or reduction of the analyte. They contain two electrodes which, when a voltage is applied, allow for oxidation or reduction of the analyte. The resulting current is proportional to the analyte concentration. The Clark electrode for the measurement of the partial pressure of oxygen (pO₂) is a classic example of an amperometric sensor.

Other varieties of electrochemical sensors are electrical conductance and enzymatic-coupled sensors. Most bedside POCT devices which measure hemocrit do so by use of an electrical conductance sensor. These sensors rely on measurements of impedance to electrical current which is related to the erythrocyte concentration. Since erythrocytes are essentially nonconducting compared with plasma, increasing hemocrit decreases the current flow in the circuit. Enzymatic-coupled sensors rely on an interaction between an enzyme in the sensor matrix and the analyte to produce an amperometric or potentiometric response which is then measured. Most glucose analyzers use the enzyme glucose oxidase to produce a reactant which is then measured amperometrically.

Most devices on the market are capable of multiple analyte measurements using a combination of these sensors to provide all of the data from a single, small, whole blood sample (Fig 2). These sensors are usually arranged along a flow through channel that allows for contact with the sample and calibration or flush solution as needed (Fig 3). In those devices not using disposable cartridges, the channel is then flushed and the waste discarded.

![Potential analytes and methods of measurement in a single POCT device.](image)

**Optical Sensors**

Optical sensors were originally developed to measure blood gases and pH using a light signal and indicator dye to measure the specific analyte of interest. The dye is separated from the blood sample by a permeable membrane to prevent clot formation and protein buildup. The sensor can use either absorbent or fluorescent modification of the light signal to determine the concentration of the analyte. This is similar to the process used in many oxygen saturation devices.

**In Vitro Instruments**

In vitro POCT devices are the most common form used at the bedside. The blood sample is drawn from the patient and then...
injected into the POCT instrument. While this does not provide true "real-time" measurements, it does allow for rapid (seconds to minutes) determination of desired variables. Most of these devices originated as single parameter instruments (Ref 6), however, most now do multiple parameters with a single sample. Two of these devices, the i-STAT Portable Clinical Analyzer (i-STAT Corp. Princeton, NJ) and the IRMA (Immediate Response Mobile Analysis) System (Diametrics, Inc., St. Paul, MN), have been evaluated extensively for their utility as portable, handheld analyzers.

To evaluate the accuracy of the i-STAT (Fig 3), it was used in an emergency department by staff without previous laboratory training (Ref 7). Samples from 574 patients were analyzed and compared with standard laboratory measurements. There was excellent correlation with urea nitrogen, glucose, and potassium. The correlations for hematocrit, sodium, and chloride were less satisfactory. A more recent study, however, found acceptable correlation in the emergency department and the stat laboratory for all analytes (Ref 8).

The IRMA has also been evaluated in the hospital setting (Fig 5). Zaloga et al analyzed 239 split blood samples in critical care patients in an intensive care unit (Ref 9). They found correlation coefficients between 0.96 to 0.99 for pO₂, pCO₂, and pH with a decrease in the turnaround time. Similarly, Wahr and colleagues reported similar results using the IRMA to assess blood gases and pH during cardiopulmonary bypass surgery (Ref 10).

A number of other devices exist and a recent review summarizes the features of each (Ref 11).

**In Vivo and Ex Vivo Instruments**

A more novel approach to the use of POCT involves in vivo and ex vivo testing devices. This includes familiar technology such as mixed venous oxygen saturation monitoring by use of pulmonary artery catheters. More novel and developing concepts such as continuous arterial blood gas monitoring through the placement of sensors directly into the artery are beginning to appear (Ref 12). Excessive expense and fragility of the systems (Fig 6) has limited their overall use and acceptance.

A more practical approach is ex vivo monitoring. This is accomplished by positioning the sensors outside of the body and allowing blood to travel from an invasive line to the sensor site before returning to the circulation. This is similar to the use of blood gas sensors placed in-line on a cardiopulmonary bypass machine. The measurements can be done continuously or on an "as needed" basis. Currently, there are no devices of this type in widespread use.
When looking at the technology currently available to perform POCT, it would appear that these devices should be extremely useful in the management of patients at remote locations. There are, however, challenges to providing this capability in the field. The environmental considerations are one of the greatest threats for the use of POCT in remote or hostile environments. Not far behind is the issue of ensuring the repeated accuracy of the equipment.

Both the IRMA and i-STAT have operating temperature ranges that can easily be exceeded in field conditions. The IRMA will operate from 15 to 30°C while the i-STAT has recently been upgraded to 10 to 30°C. These temperature ranges also apply to the cartridges. In our experience, this is one of the more common operating errors encountered when using the IRMA outside of the hospital. When working in a cold environment, like the inside of a C-130 at altitude, it becomes necessary to carry the disposable cartridges for both systems inside a flight suit in order to ensure that they remain within the temperature operating range. Both devices are capable or working in a low humidity environment down to 0%, however, their upper limit is around 65% according to the manufacturer’s recommendations. Barometric pressure should not be a problem under most operating conditions. The IRMA is reported to function from 350 to 900 mm Hg (59-86 kP). An onboard barometer calibrates the system for the current barometric pressure prior to each use. The i-STAT has recently completed testing at the Armstrong Laboratory, Brooks AFB, TX where there were no reported problems with sample attached to injection port. The IRMA has not completed testing at this time

Evaluating the repeated accuracy of these devices is an important part of using the equipment. The process of quality checking involves the method whereby the analyst tests the equipment through a standardized routine to document the accuracy of the measurements. Common laboratory practice frequently requires multiple test samples of known quantity to be run on the system in order to ensure accuracy. This time consuming process has been greatly simplified with POCT devices. In fact many of the current systems do not require the use of any reagent based calibration samples. Electronic calibration is performed using a calibrated cartridge and accomplished in seconds to minutes. A second method of calibration involves the placement of a calibration gel or liquid on each disposable cartridge such that a calibration is performed before each sample. The calibration gel or fluid is then replaced by the actual sample during the testing phase. Some systems such as the i-STAT and the IRMA use a combination of these methods with an option to perform independent liquid calibration. This combination of calibrations should be easy to perform even under field conditions and will allow for the smooth operation of the devices.

Discussions about the clinical utility of POCT in a nontraditional environment revolve around not only its usefulness in decision making, but also its impact on therapeutic turnaround time and outcomes. Whatever role POCT has in improving the care our patients receive when we are far from the traditional hospital should be based on sound evidence-based medical decisions. When deciding about the usefulness of POCT derived data, we are not looking at a turnaround time based on minutes, but on hours or even days if it is not available. Clinical decisions such as the need or urgency of aeromedical evacuation from a remote location may be better guided if hard evidence, rather than the “worst case” scenario, is available for review. The availability of a simple blood test, using POCT principles, to rule out an acute myocardial infarction (such as a test for troponin-I) can be combined with the exam and electrocardiogram to risk stratify the patient with atypical chest pain. Ultimately, POCT is only useful if you have the capacity to use the information for establishing diagnosis, instituting treatment, or performing triage. If, after careful review, POCT appears to offer benefits for use in the field, then the cost factor needs to be considered.

Point-of-care testing is not inexpensive. A single multiparameter device can run over $5000 with a cost of $3-9 for each cartridge. The addition of a short half-life for the cartridges can add significantly to the overall cost of maintaining this capability. This must be weighed against the information gained when POCT is used and implemented properly.

The literature looking at the implementation of POCT in the field is very limited. There are only two studies which have
taken this type of analytical capability out of the hospital and into the field setting. Both of these studies examined the utility of the i-STAT in this role. One concentrated on its use in an ambulance service and the other in a helicopter rescue unit.

Tortella et al examined the consistency of measurements obtained when in the field (Ref 13). In this study, all samples were collected in the back of a moving ambulance and run on two i-STAT units while en route. An additional specimen was saved for later testing in the emergency department on the same units and an additional i-STAT analyzer. The samples showed excellent consistency between those obtained and run “on the move” and those run in the emergency department. Of note, the authors reported having problems with operation of the units in the field due to cold temperatures and they had to design a special insulated bag to protect the analyzers.

In the second study, Herr and colleagues reported on their experiences using the i-STAT during helicopter transport of 81 patients (Ref 14). Samples were simultaneously run through the analyzer and stored for later analysis at the main laboratory. Of the 332 samples run at both sites, only 1.8% did not correlate. No therapeutic decisions were made based on those measurements which did not show good correlation. In this study, POCT led to the administration of insulin in two diabetics and the administration of glucose to another. Since these helicopter flights also had the capability to administer blood products, the discovery of a low hematocrit leading to transfusion was the most common treatment received on the basis of POCT (16 patients or 19.8% of all patients). Overall, 24.7% of all patients received some form of treatment based on the results of POCT testing. Of note, the problems with temperature reported in this study were similar to those reported in the preceding one, underlining the significance of environmental factors in the performance of these units.

CONCLUSIONS

Currently, POCT is a reality in our hospitals and its use is going to continue to expand in the future. Under controlled environmental conditions, POCT can be used in the field. Most notably, problems with the extremes of temperature are going to require innovative solutions in order to get the most from these devices. Additional improvements may correct these shortfalls since it is a recognized limitation for expanding its use outside the hospital.

If POCT can help guide the management and triage of our most critically ill patients as they flow through the military medical system, it will quickly establish itself as a new paradigm. For the U.S. military medical community, if we are going to provide essential care forward with early evacuation of the “stabilized” patient, POCT will be immensely useful in maintaining a continuum of en route care that currently does not exist in its full capacity.

REFERENCES